Ekaterina Golubeva
ZHAW

Track Module 1
24.11.2022

First visit of the Intensive Care Unit at USZ

with Jan Bartussek

Infrastructure:

There are 6 Intensive Care Units at the USZ having in total 64 beds:

- Focus in cardiac and vascular surgery
- Focus on internal medicine
- Focus on neurosurgery
- Focus on burns
- Focus on traumatology
- Focus on visceral, thoracic and transplant surgery

In each ward, there are many detecting, recording, medical equipment such as MetaVision Suite (from Clinical Information Systems), ventilators to provide patients with oxygen, perfusors for medication, electrodes collecting signals from the patients, blood gas analyzers and many more.
The Patient Data Management System collects one value per minute for each of the following parameters: heart frequency, arterial blood pressure, peripheral arterial pressure, breathing frequency, central venous pressure. These values are constantly monitored.

Data:

ICU collects data in PDMS, whereas all the detailed information about the clinical history of the patients such as their diagnosis are in KISIM (digital platform for the whole clinic).
Real world data is often messy. In our case, signals are corrupted by artificial intervention for treatment (e.g. supply with oxygen) in addition to the biological signals from the patient. The analysis of the data can only be as good as the quality of data is. Therefore, data preprocessing is very important.

Delirium:

Delirium, the syndrome of interest in our research group, is a neurological disorder that translates as disturbance of brain signal processing. In patients' experience it could be described as locked in a dream, waking up from which, they don't have any memory of what they did while being in state of delirium. In general, 25% of patients of total ICU patients develop delirium following an operation, a specific medication or for other reasons. Here are some risk factors that raise the probability for a patient to suffer from delirium:

- Age (the older the patient, the more probable it is to have delirium)
- Infections (brain infections, encephalopathy, and others)
- Medication
- Surgery, anesthesia
- Fluid disbalance

If we modelled the neurological signal as a function of the amount of neurotransmitters and the

sensitivity of a neuron, these two variables would be altered in delirium. The state of patients with delirium can vary from being sleepy to being physically aggressive. It can be completely gone after treatment or induce long term consequences such as dementia. Delirium state may last from several hours to several days. In cases of severe delirium and aggressivity, patients get sedated (e.g. put in coma), in milder cases drugs are used (e.g. dexmedetomidine, called Dexdor).
To quantify the mental/physical status of the patient certain criteria are used. For each parameter, points are gathered and turn into a score which then becomes a predictor for mortality within 24h.
For delirium the following criteria are used (ICDSC):

- Altered level of consciousness
- Inattention (capacity to follow simple commands, focus)
- Disorientation
- Hallucination
- Psychomotor agitation or retardation
- Sleep wake cycle disturbance
- Inappropriate speech
- Fluctuations in symptoms

The threshold of score to be considered delirium is ≥ 4 out of 8.
Some patients with delirium at the ICU have other life-threatening conditions. Delirium, being a side effect, it is not systematically documented. On the other side, some patients have a positive delirium score but are not diagnosed with delirium because these symptoms are caused by a brain disease (e.g. encephalopathy). Therefore, we must distinguish patients with positive score and positive diagnosis.

Hyper/Hypo-oxemia:

The excess or lack of oxygen is assumed and studied as a correlated factor with delirium. Indeed, certain concentration of reactive oxygen species (chemicals as a byproduct of oxygen) cause cell damage or signal alteration. The harmful effect can be a result of both hyperoxemia, hypoxemia or a combination of both. These factors can be regulated by the doctors via a ventilator.

Ethics:

Patients are protected by law, so I am not allowed to take pictures, share their names or any personal information. It is not allowed to copy real data from the clinical archives, therefore for the purpose of exercise, I will have to work with synthetic data that doesn't belong to any patient.

Remaining questions:

- How do ROS (reactive oxygen species) affect the brain or how hyper/hypo-oxemia are related to delirium?
- What are the C-ROS (antioxidants) and how can we regulate their production?

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Track Module 1
01.12.2022

Second visit of the USZ

with Jan Bartussek

1) Critical reading of a scientific paper

Lessons learnt:

- Correlation is not causality. In medical research, we mostly deal with available data from observations. We cannot reproduce experiments as it is done with animal research for example. Therefore, we cannot prove causality by specifically designed experiment. There are a lot of factors affecting human health and one cannot easily distinguish what is a reason for a certain condition, we can only observe correlations.
- A scientific paper is tedious to read. Advice on starting to read: abstract, figures, conclusions, then methods.
- Sample sizes should be large enough to have statistically significant results. When we have groups with very different sample sizes, we have to weight the data so different groups can be compared.
- Compare the results of the study with the common scientific knowledge. Example from the study (Acute and postacute sequelae associated with SARS-CoV-2 reinfection): after first infection, the immunity should be stronger, not weaker as the study suggests.
- There should be a coherence between findings and the conclusion. Example from the study (Acute and postacute sequelae associated with SARS-CoV-2 reinfection): the study shows that the vaccines didn't influence the reinfection, but conclusion suggests improving prevention.

2) Processing synthetic data:

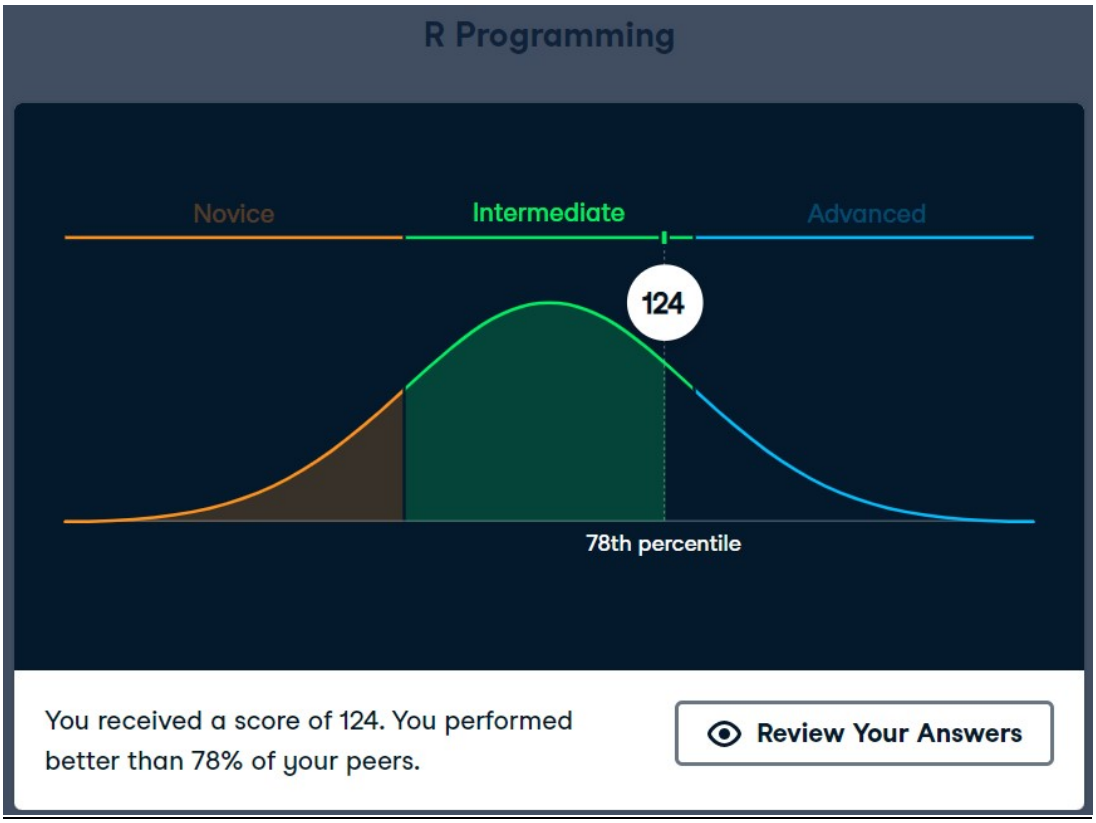
I was given a set of fictive data from patients containing patient id, Delirium diagnosis, ICDSC score and information about their alcohol consumption and smoking habits. To process data and do some statistical analysis on it, I first tried to tidy it by removing missing values, taking out the drug columns because there is no information, setting variables to the factor type. I then calculated the proportions of positive and negative delirium diagnosis and score. Then I plotted packyears against alcohol consumption with a color code corresponding to diagnosis to study the hypothesis that there's a positive correlation between alcohol and/or smoking on the delirium score/diagnosis.

3) Programming skills assessment:

I was suggested to evaluate my R/Python skills with the datacamp platform following the courses and taking the assessment quizzes in

Introduction to R
Intermediate R
Introduction to Python

Results from programming skills assessment on data camp



Knowledge Summary

Your strengths and skill gaps are based on how you performed within each subskill in the assessment.

Strengths

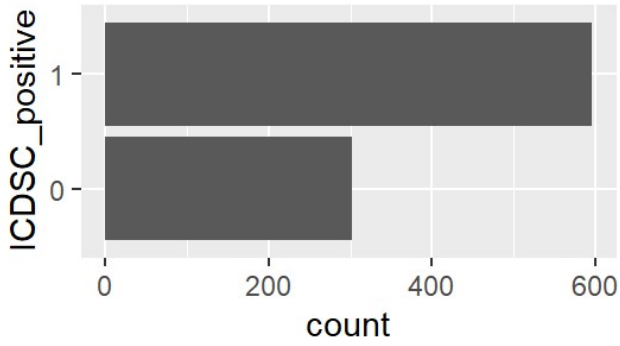
Data Structures	5/5
Object-Oriented Programming	1/1
Loops, Control Flow	1/1

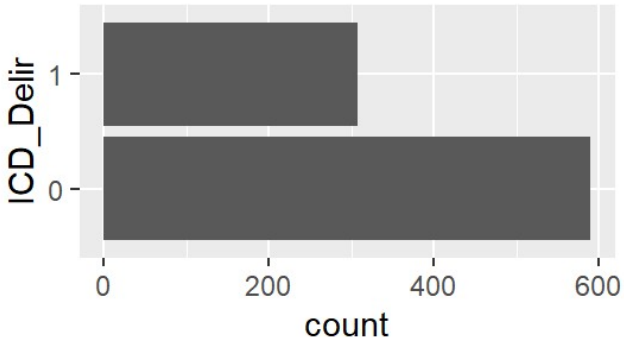
Skill Gaps

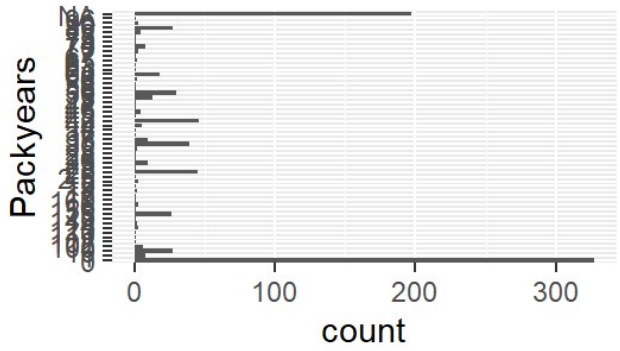
Functional Programming	0/4
Efficient Coding	0/1
Functions	0/1

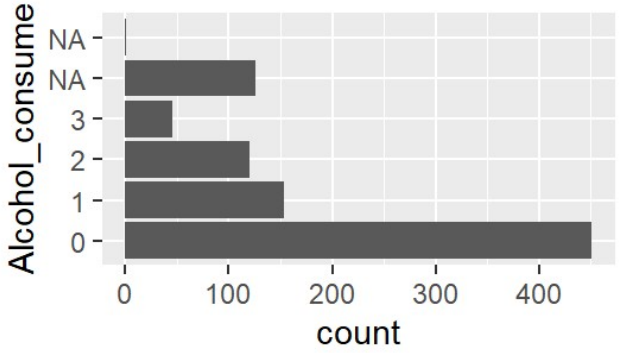
Plots from synthetic delirium data processing:

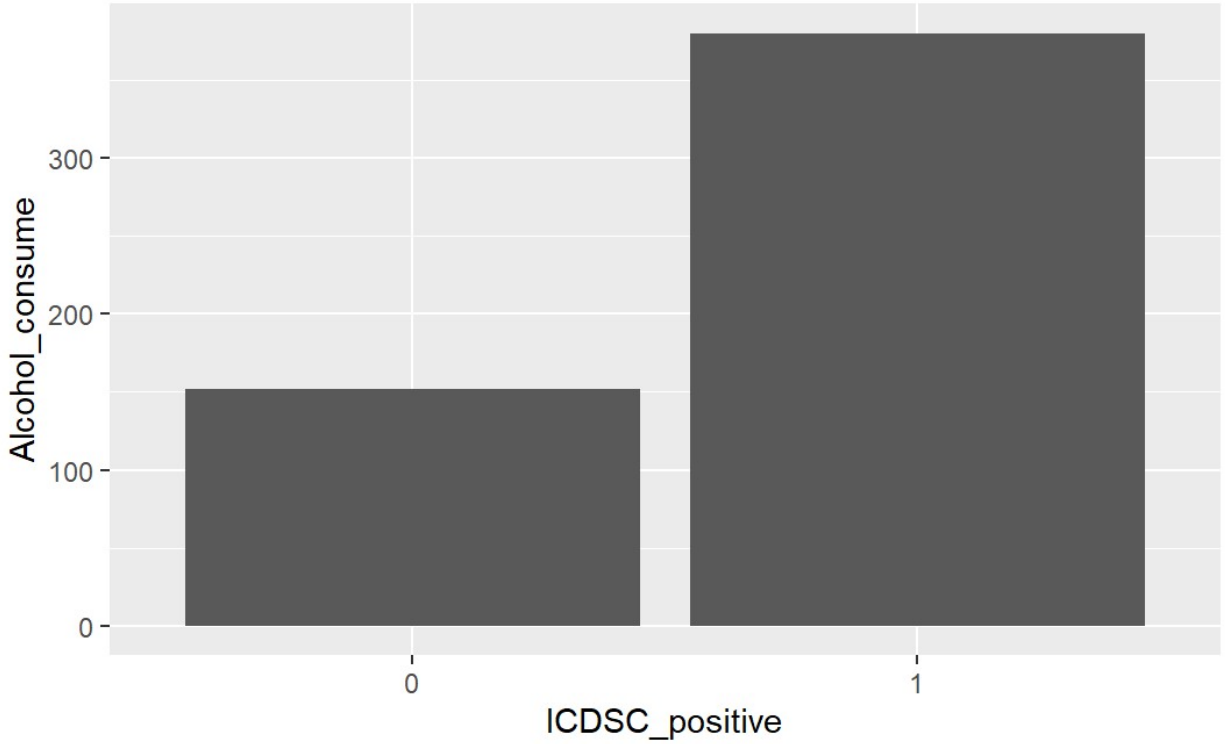
General Statistics

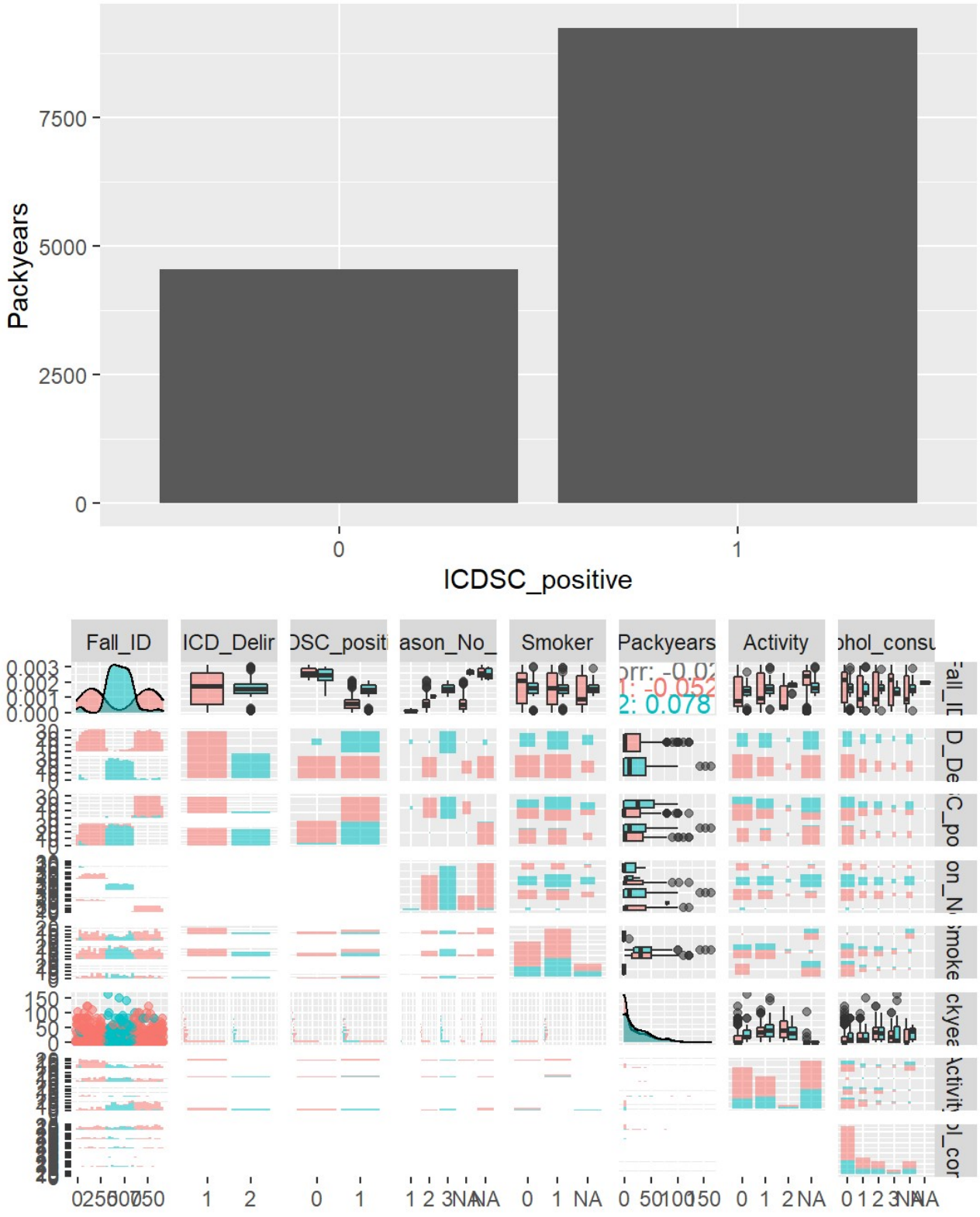


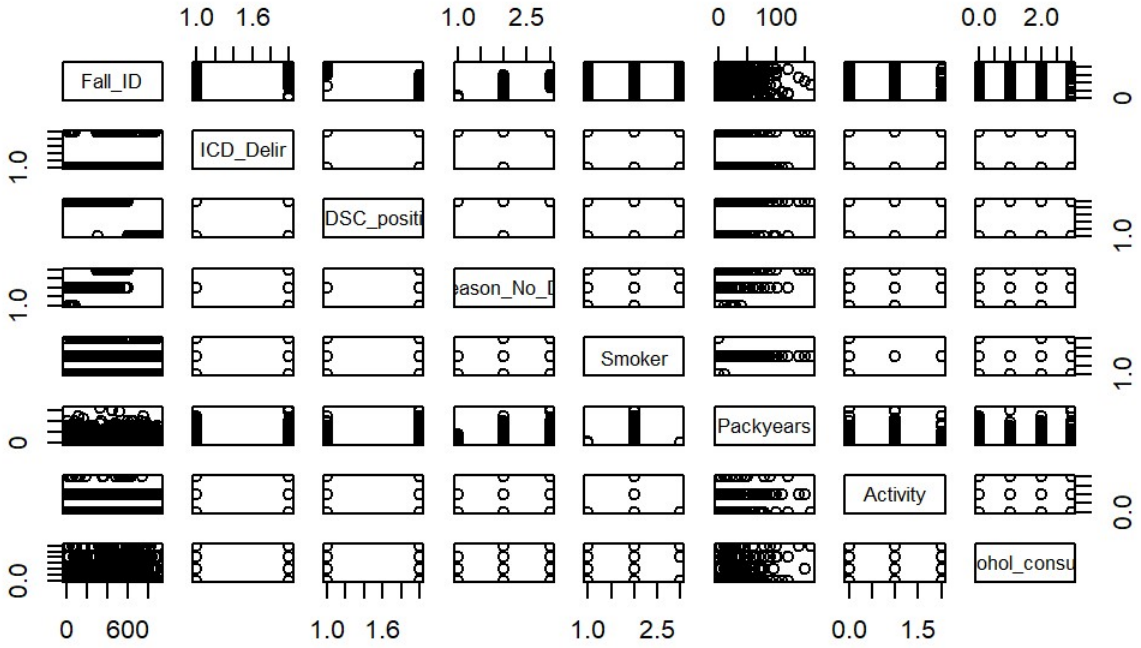


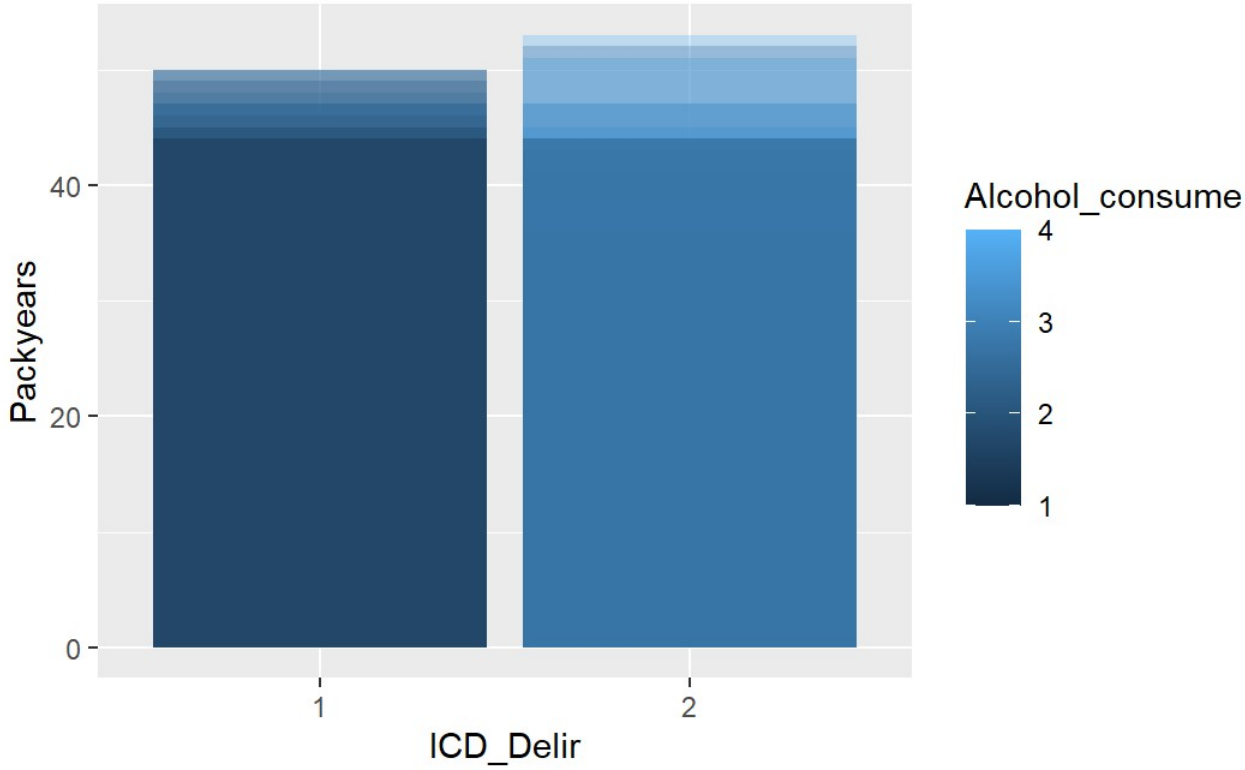







Packyears
7500
5000
2500
0
0
1
ICDSC_positive
Fall_ID
ICD_Delir
DSC_positi
ason_No_
Smoker
Packyears
Activity
hol_consu
0.003
0.002
0.001
0.000
1: -0.052
2: 0.078
150
100
50
0
0 25 50 75
1 2
0 1
1 2 3 NA
0 1 NA
0 50 100 150
0 1 2 NA
0 1 2 3 NA


Fall_ID
ICD_Delir
DSC_positi
eason_No_D
Smoker
Packyears
Activity
ohol_consu
1.0 1.6
1.0 2.5
0 100
0.0 2.0
0 600
1.0 1.6
1.0 2.5
0.0 1.5


Packyears
ICD_Delir
Alcohol_consume
40
20
0
1
2
4
3
2
1

Ekaterina Golubeva
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Track Module 1

08.12.2022

3rd day at the USZ

with Jan Bartussek

Further plots of the m synthetic delirium data. I split the data set into 3 groups and studied histograms for Alcohol consumption, Smoking activity and Packyears for each of the groups.

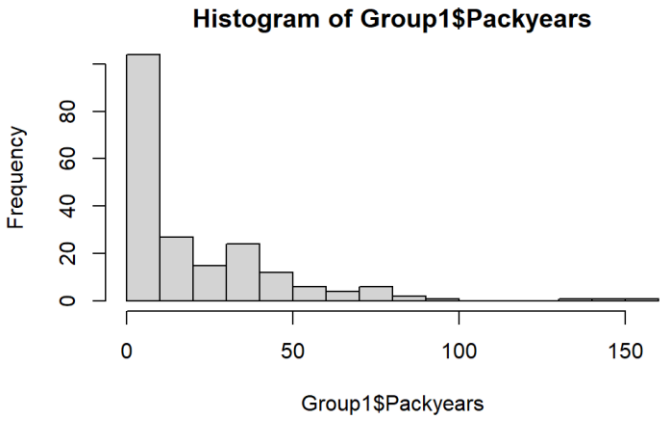
Group1 = positive diagnosis, positive score

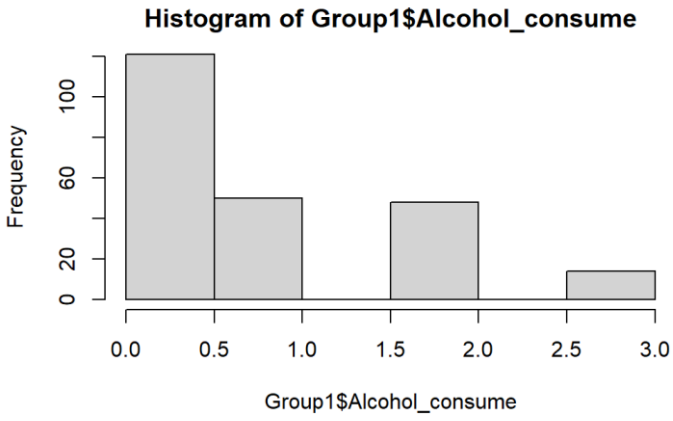
Group2 = negative diagnosis, positive score

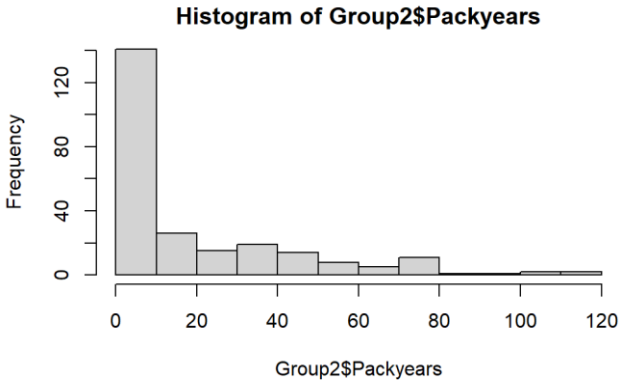
Group3 = negative diagnosis, negative score

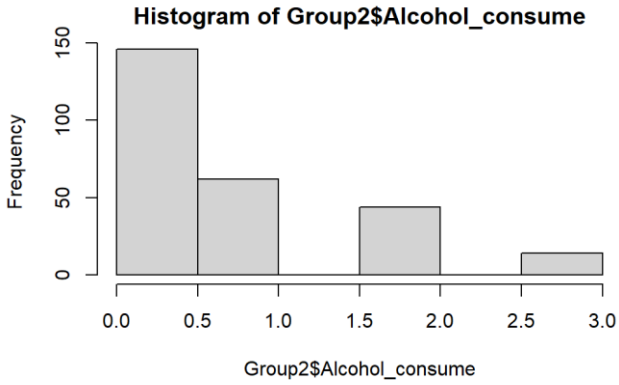
Lessons learnt:

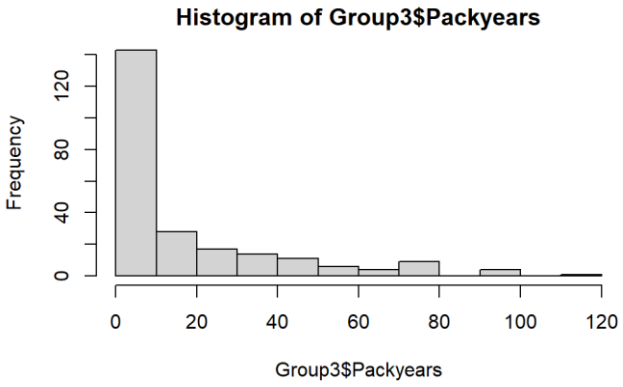
- It is easier to first plot histograms for each of the factors before plotting their interactions.
- Normalize the frequency to compare plots or make sure the group sizes are equal.
- Translate frequency into density to see percentages.
- There might be inconsistencies with the number of patients who claim they don't consume alcohol: they might have stopped drinking but still exhibiting same behaviors as when they were still drinking alcohol. There might also be incorrect correlations (or their absence) between patients with delirium and no alcohol consumption as they might be suffering form alcohol withdrawal delirium instead of the delirium defined earlier (neurological phenomenon).
- It is also useful to keep in mind that nicotine presence affects drug efficiency. Therefore, patients who smoke need more sedation medication in general.
- Further work could be done to study the relationships between the three groups using statistical tests such as chi squared test.

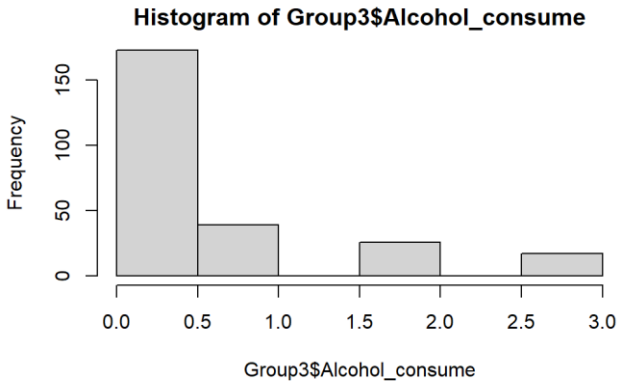

Histogram of Group1$Packyears
Frequency
0
20
40
60
80
0
50
100
150
Group1$Packyears

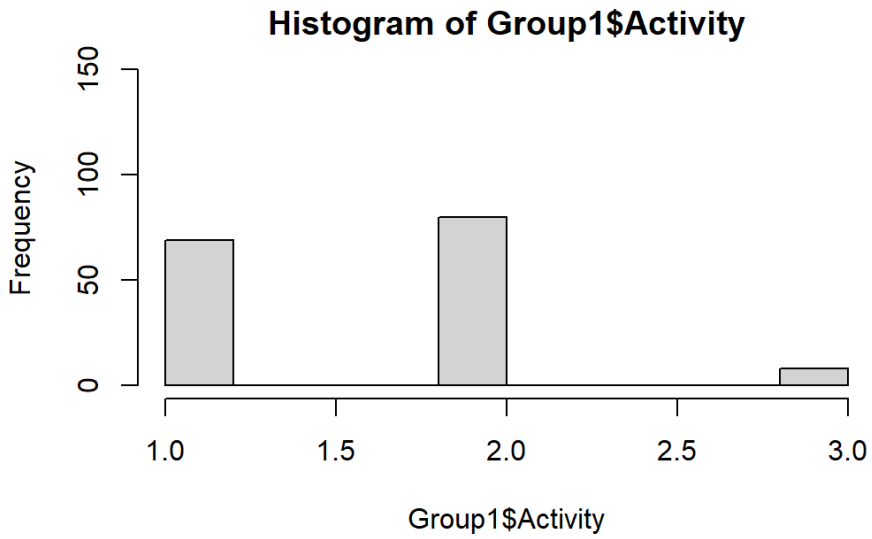

Histogram of Group1$Alcohol_consume
Frequency
0
20
60
100
0.0
0.5
1.0
1.5
2.0
2.5
3.0
Group1$Alcohol_consume

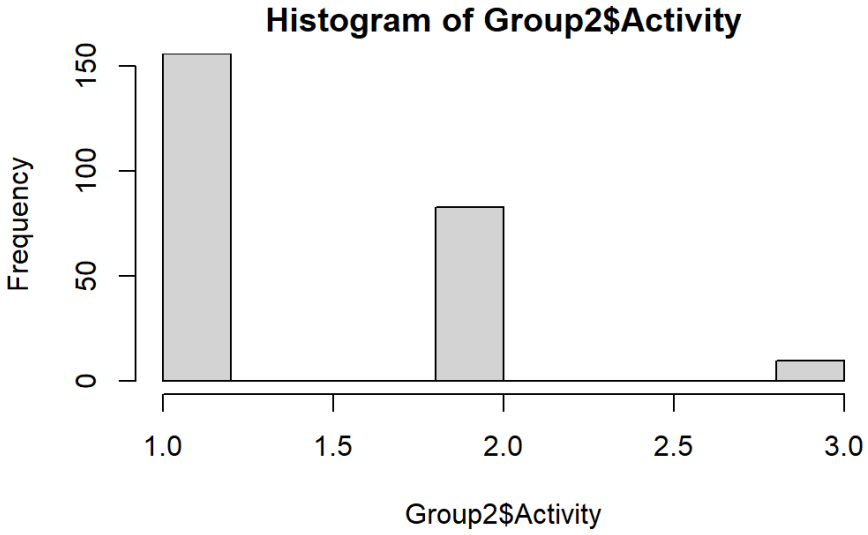

Histogram of Group2$Packyears
Frequency
0
40
80
120
0
20
40
60
80
100
120
Group2$Packyears

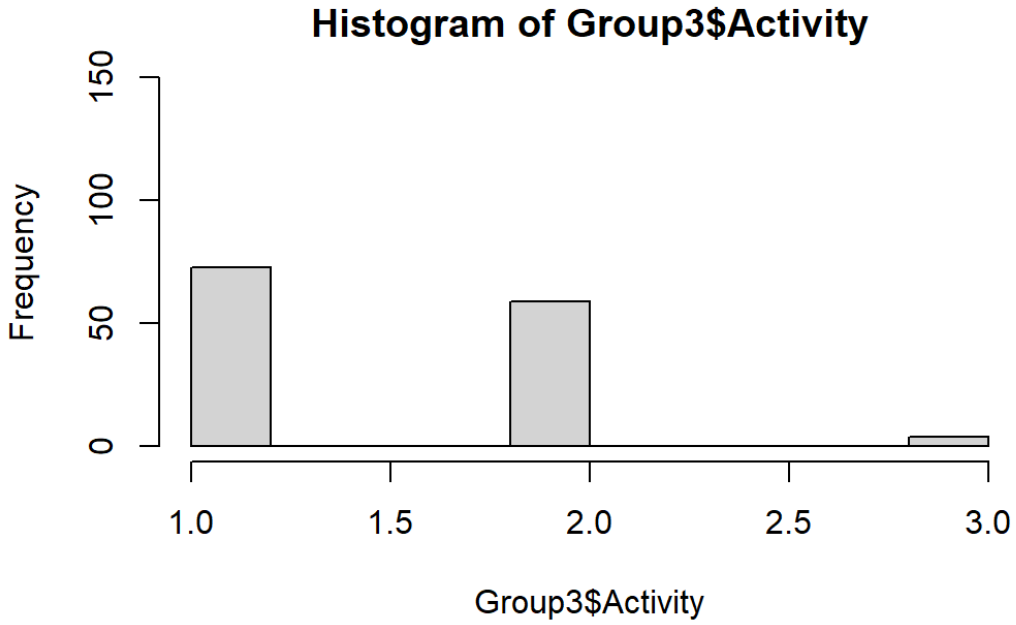

Histogram of Group2$Alcohol_consume
Frequency
0
50
100
150
0.0
0.5
1.0
1.5
2.0
2.5
3.0
Group2$Alcohol_consume

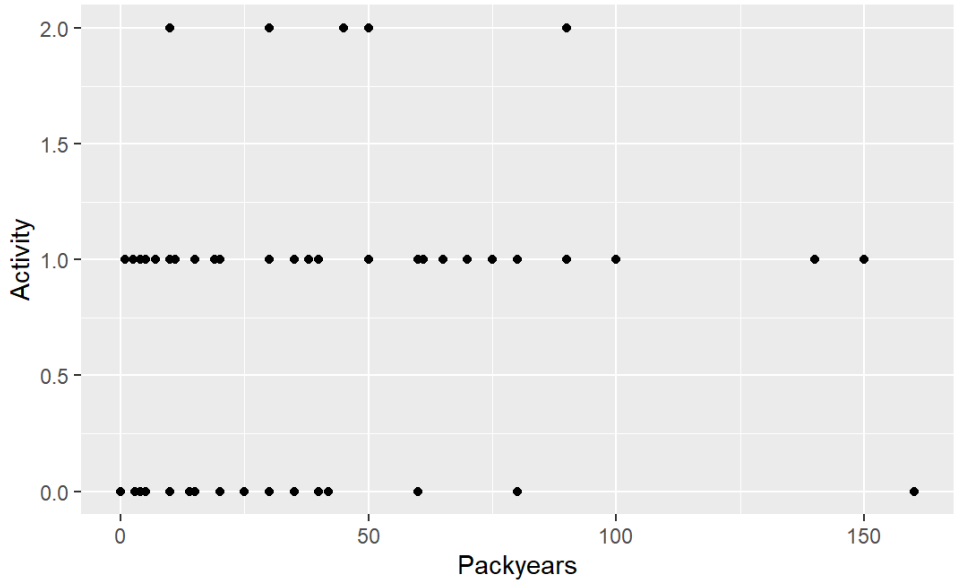

Histogram of Group3$Packyears
Frequency
0
40
80
120
0
20
40
60
80
100
120
Group3$Packyears

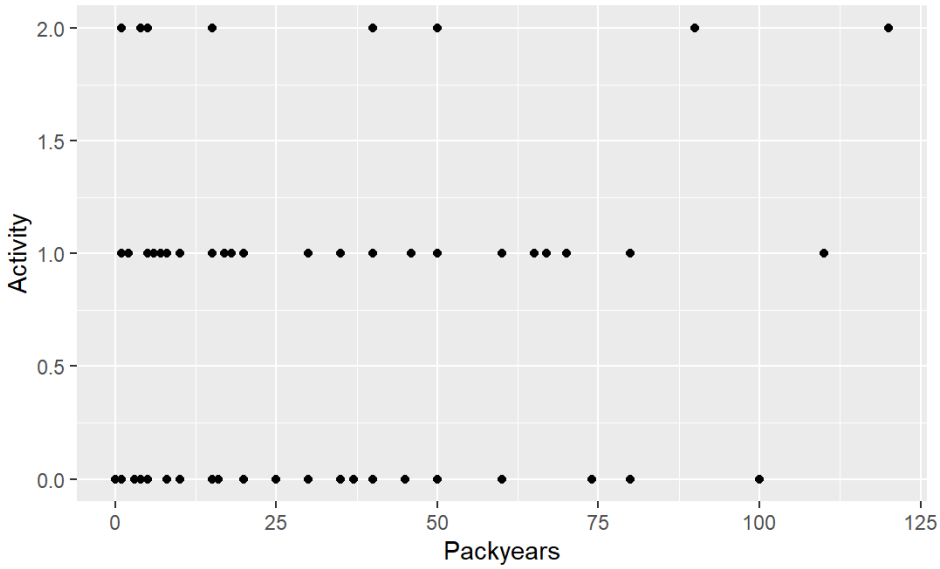

Histogram of Group3$Alcohol_consume
Frequency
0
50
100
150
0.0
0.5
1.0
1.5
2.0
2.5
3.0
Group3$Alcohol_consume

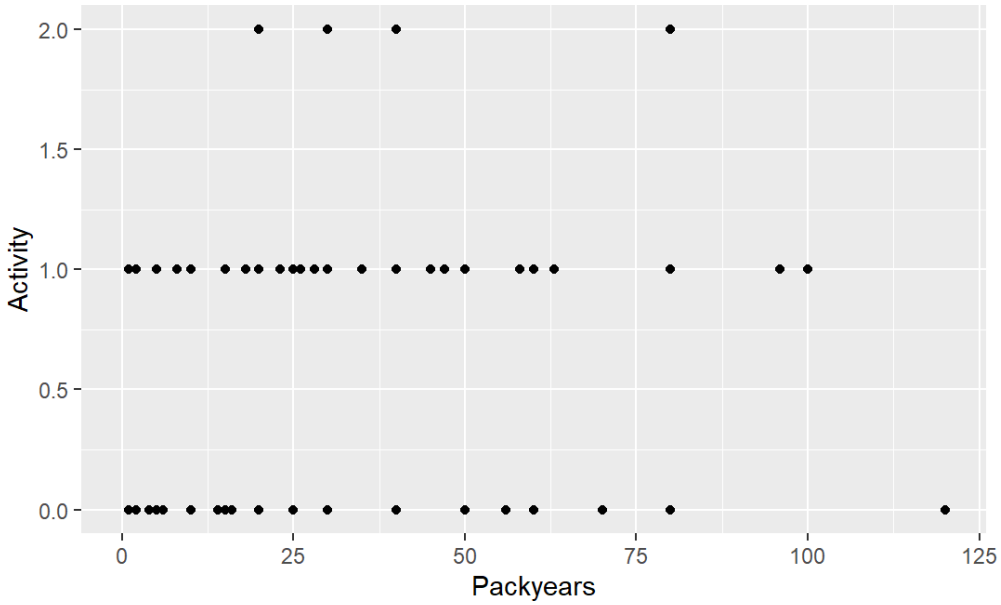

Histogram of Group1$Activity
Frequency
0
50
100
150
1.0
1.5
2.0
2.5
3.0
Group1$Activity

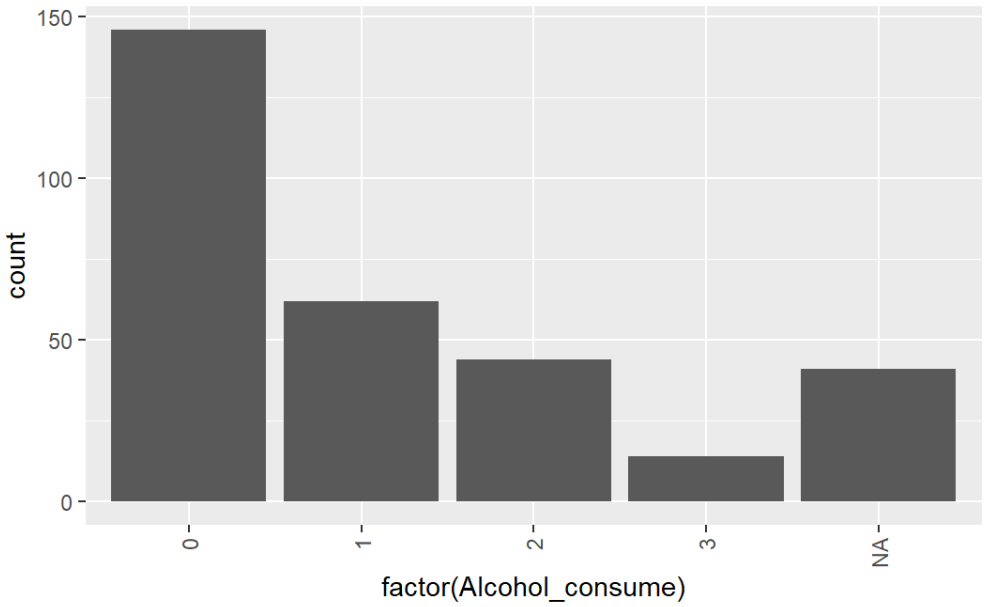

Histogram of Group2$Activity
Frequency
0
50
100
150
1.0
1.5
2.0
2.5
3.0
Group2$Activity

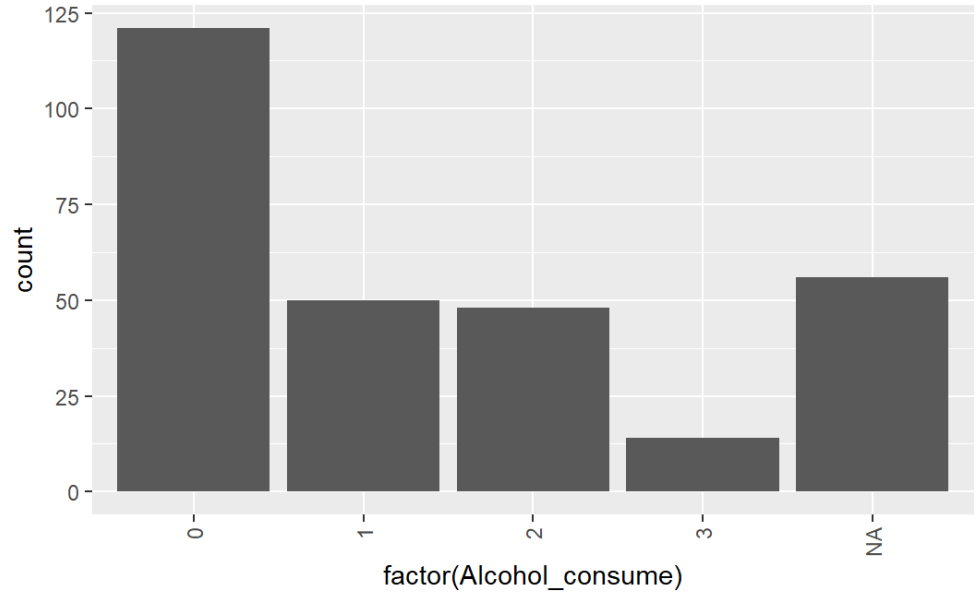

Histogram of Group3$Activity
Frequency
0
50
100
150
1.0
1.5
2.0
2.5
3.0
Group3$Activity

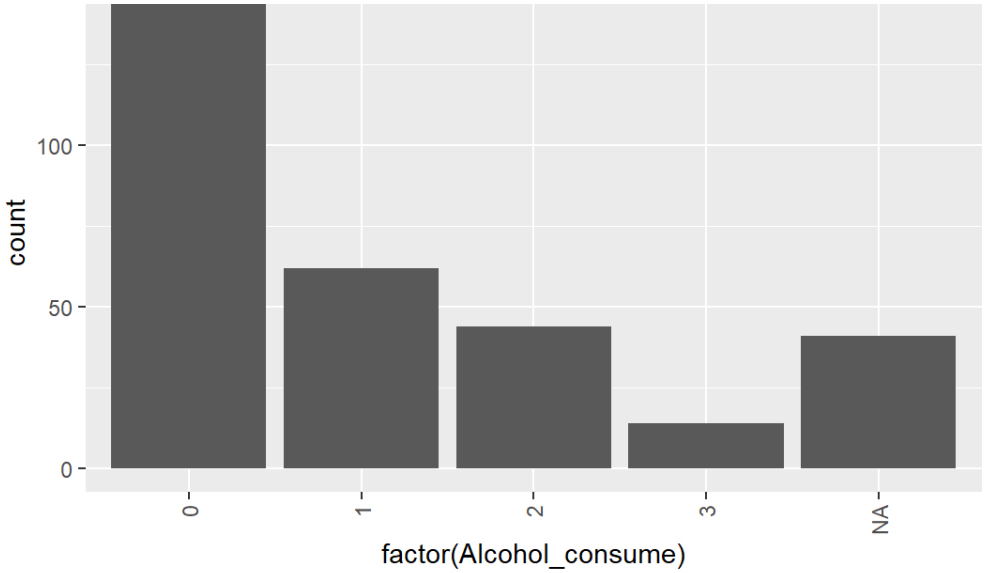

Activity
2.0
1.5
1.0
0.5
0.0
0
50
100
150
Packyears

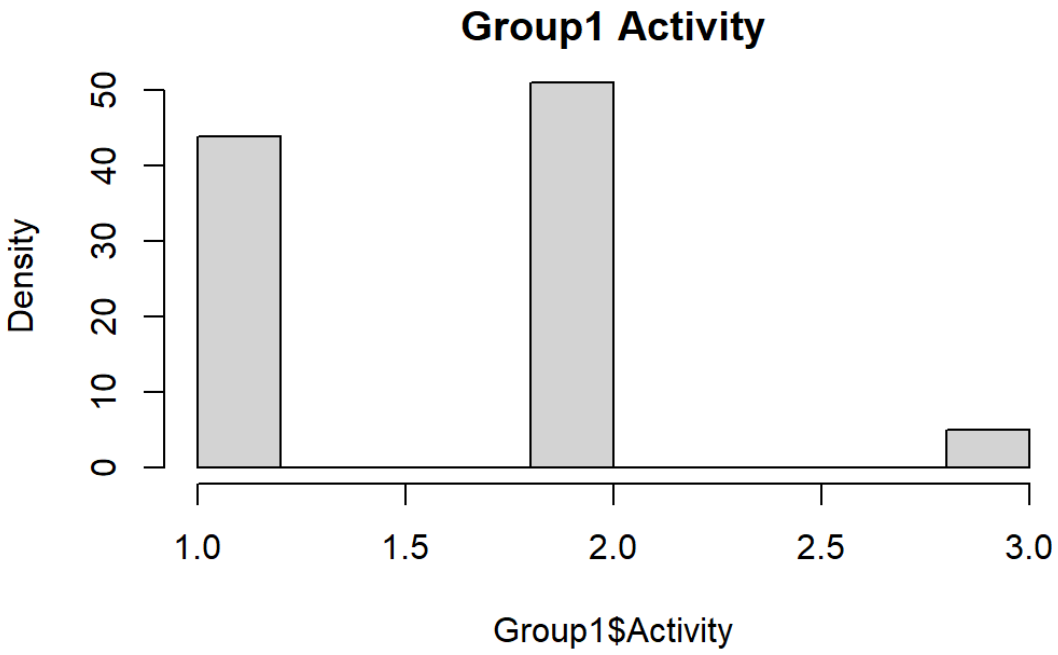

Activity
2.0
1.5
1.0
0.5
0.0
0
25
50
75
100
125
Packyears

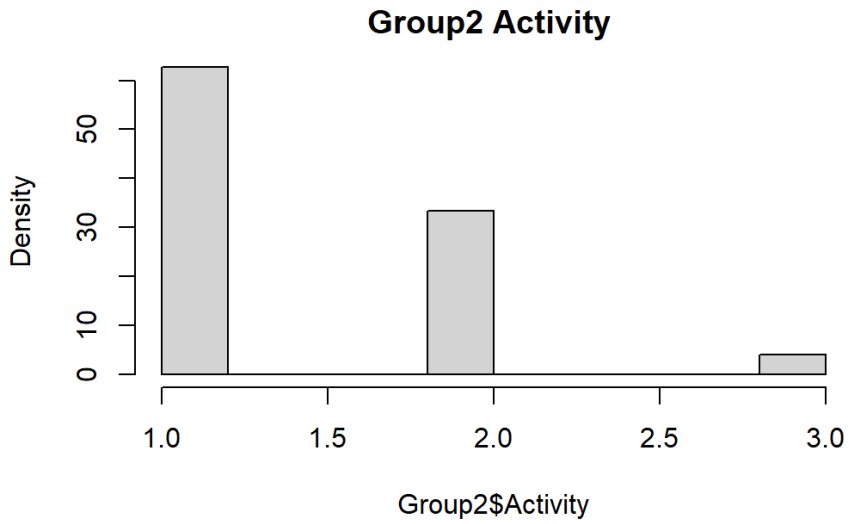

Activity
2.0
1.5
1.0
0.5
0.0
0
25
50
75
100
125
Packyears

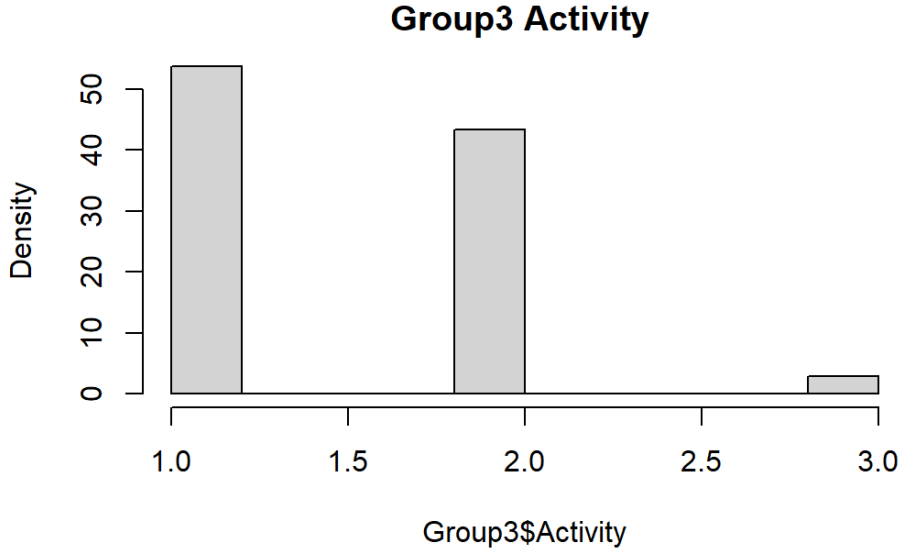

150
100
50
0
count
0
1
2
3
NA
factor(Alcohol_consume)


125
100
75
50
25
0
count
0
1
2
3
NA
factor(Alcohol_consume)


100
50
0
count
0
1
2
3
NA
factor(Alcohol_consume)


Group1 Activity
Density
0
10
20
30
40
50
1.0
1.5
2.0
2.5
3.0
Group1$Activity


Group2 Activity
Density
0
10
30
50
1.0
1.5
2.0
2.5
3.0
Group2$Activity


Group3 Activity
Density
0
10
20
30
40
50
1.0
1.5
2.0
2.5
3.0
Group3$Activity